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| 10/555,078 | 04/05/2006 | Tai-Tung Yip | CIPH-0015 | 9106 |

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WOODCOCK WASHBURN LLP
ONE LIBERTY PLACE
46TH FLOOR
PHILADELPHIA, PA 19103

| EXAMINER | |
|---|---|
| LAM, ANN Y | |

| ART UNIT | PAPER NUMBER |
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| 1641 | |

DATE MAILED: 09/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/555,078 | YIP ET AL. | |
| | Examiner | Art Unit | |
| | Ann Y. Lam | 1641 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *28 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-11,20,24,35,43 and 48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,20,24,35,43 and 48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/12/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11, 43 and 48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11, line 2, recites "the target antigen". The claim lacks antecedent basis for this limitation.

Claim 43, lines 1-2, recites "measuring modified forms of an anti-target antigen antibody in an antibody reagent for a target antigen immunoassay". It is not clear as to what is being measured—the antibody, i.e., the "anti-target antigen antibody", or the "target antigen". Clarification is requested. For examination purposes, the term will be interpreted to be measuring antibody.

Claim 48, recites in the preamble, "A method for discovering polypeptides that interact with target antigen". However there is not such step of discovering polypeptides that interact with the target antigen in the body, nor is it clear how the polypeptides that interact with the target antigen is discovered.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4, 6, 7, 9-11, 35 and 43 are rejected under 35 U.S.C. 102(e) as being anticipated by Nelson et al., 6,974,704.

As to claim 1, Nelson et al. disclose a method comprising

capturing polypeptides (e.g., antibodies, see col. 17, line 55; or antigen, see col. 17, line 54, which may be an allergen, col. 6, lines 26-30, which carry proteins, see col. 6, lines 3-7, i.e., polypeptides) from a sample (col. 12, line 59 – col. 13, line 8),

wherein the polypeptides comprise target antigen and at least one modified form of target antigen (col. 13, lines 2-3, and col. 8, lines 19-16);

and specifically measuring captured target antigen (col. 12, lines 63-64; and col. 11, lines 47-56; and col. 17, lines 38-57).

As to claim 2, the polypeptides are captured with an antibody (col. 2, lines 62-63). (The antibodies capturing antigens, see col. 17, line 2, line 63, and col. 6, lines 26-30, lines 3-7).

As to claim 3, the polypeptides are captured with chromatographic sorbent (e.g., agarose beads, col. 8, lines 53-56, and col. 20, line 53).

As to claim 4, the method further comprises specifically measuring at least one modified form of target antigen (col. 12, lines 63-64; and see also col. 17, lines 38-57).

As to claim 6, the captured polypeptides are measured by mass spectrometry (col. 12, lines 61-65, and col. 17, lines 38-44).

As to claim 7, the captured polypeptides are measured by affinity mass spectrometry (col. 13, lines 3-8, disclosing the capture of the polypeptide through an affinant, col. 12, lines 61-65, and col. 17, lines 38-44, disclosing mass spectrometry).

As to claim 9, the sample is a subject sample and the method further comprises: correlating the detected target antigen with a clinical parameter in the subject col. 17, lines 51-53).

As to claim 10, the clinical parameter is presence or absences of a disease associated with the target antigen (col. 17, lines 51-53).

As to claim 11, Nelson et al. discloses capturing at least one modified form of a target antigen polypeptide from a sample (col. 13, lines 2-8); and specifically measuring the at least one captured modified form of the target antigen polypeptide (col. 12, lines 61-65).

As to claim 35, Nelson et al. discloses a method for qualifying an immunoassay calibrator for a target antigen immunoassay comprising:

providing an immunoassay calibrator for a target antigen immunoassay, wherein the calibrator comprises a designated concentration of target antigen (col. 13, lines 4-5);

capturing polypeptides from the calibrator with an anti-target antigen antibody (col. 13, lines 4-5);

and specifically measuring an amount of at least one polypeptide selected from target antigen and modified form of the target antigen captured by the antibody (col. 12, lines 61-65), whereby the measured amount provides an indication of the quality of the immunoassay calibrator (col. 14, lines 42-45, disclosing calibration using the internal reference species; and see also col. 15, lines 5-9, disclosing comparison of signals of an internal reference species to directly quantify an analyte).

As to claim 43, Nelson et al. teach a method comprising measuring modified forms of an anti-target antigen antibody in an antibody reagent for a target antigen immunoassay (see col. 17, lines 51-57, disclosing the determination of antibody concentration).

Claim 20 is rejected under 35 U.S.C. 102(b) as being anticipated by Anderson et al., 6,267,722.

Applicant claims method comprising: providing a learning set comprising a plurality of data objects representing subjects, wherein each data object comprises data representing a specific measurement of target antigen from a subject sample and a clinical parameter of the subject; and determining a correlation between specific measurement of target antigen and the clinical parameters. Anderson et al. disclose these limitations by teaching that signals from a diagnostic test is processed using data

processing software employing data reduction and curve fitting algorithms to give either a positive or negative result, or a quantitative determination of the concentration of analyte in the sample, which is correlated with a result indicative of a risk or presence of a disease or disorder and that the entire procedure is automated and/or computer-controlled (col. 3, lines 25-37).

Claims 1-7, 9, 10 and 48 are rejected under 35 U.S.C. 102(e) as being anticipated by Singh et al., 2002/0034827.

As to independent claim 1, Applicant claims method comprising capturing polypeptides from a sample wherein the polypeptides comprise target antigen and at least one modified form of target antigen; and specifically measuring captured target antigen. As to claim independent 11, Applicant claims capturing at least one modified form of a target antigen polypeptide from a sample; and specifically measuring the at least one captured modified form of the target antigen polypeptide. As to independent claim 43, Applicant claims a method comprising measuring modified forms of an anti-target antigen antibody in an antibody reagent for a target antigen immunoassay.

Singh et al. disclose these limitations by teaching that any protein can be subjected to co- and post-translational modifications such as acetylation, phosphorylation, methylation, etc. (paragraph [0080]). Singh et al. further teach that an antibody will capture not only the protein against which it has been raised, but also protein isoforms (i.e., proteins that share similar epitopes but are modified at different

sites. Singh et al. teach that if the isoform is recognized by the detection antibody, it will be quantitated along with the "parent protein". Singh et al. further teach that after fluorescence measurement, the proteins may be captured by probes and subjected to mass spectrometry analysis (paragraph [0081]), and that characterization of the proteins by mass spectrometry identifies the different post-translation modifications [0082]).

As to claim 2, the polypeptides are captured with an antibody (paragraph [0065])

As to claim 3, the polypeptides are captured with chromatographic sorbent (paragraph [0065]).

As to claim 4, the method further comprises specifically measuring at least one modified form of target antigen (paragraphs [0065] and [0081]).

As to claim 5, the method further comprises capturing and measuring a polypeptide interactor of the target antigen (see paragraph [0080], disclosing that the modification of the protein analyte may be phosphorylation—the phosphor in this case is deemed to be the claimed interactor and it is indirectly measured).

As to claim 6, the captured polypeptides are measured by mass spectrometry (paragraph [0028]).

As to claim 7, the captured polypeptides are measured by affinity mass spectrometry (paragraph [0028] and [0065]).

As to claim 9, the sample is a subject sample and the method further comprises: correlating the detected target antigen with a clinical parameter in the subject (paragraph [0027]).

As to claim 10, the clinical parameter is presence or absences of a disease associated with the target antigen [paragraphs (0027], and [0164]).

As to claim 48, Applicant claims a method for discovering polypeptides that interact with target antigen comprising: capturing target antigen from a sample with a biospecific capture reagent; removing molecules that are not bound to the biospecific capture reagent or the target antigen; and measuring molecules bound to the captured target antigen. Singh et al. disclose these limitations by teaching that any protein can be subjected to co- and post-translational modifications such as acetylation, phosphorylation, methylation, etc. (paragraph [0080]). Singh et al. further teach that an antibody will capture not only the protein against which it has been raised, but also protein isoforms (i.e., proteins that share similar epitopes but are modified at different sites. Singh et al. teach that if the isoform is recognized by the detection antibody, it will be quantitated along with the "parent protein". Singh et al. further teach that after fluorescence measurement, the proteins may be captured by probes and subjected to mass spectrometry analysis (paragraph [0081]), and that characterization of the proteins by mass spectrometry identifies the different post-translation modifications [0082]). The phosphor, in the case of phosphorylation as the modification (paragraph [0080], is deemed to be the claimed interactor and it is indirectly measured. The removing of unbound material is disclosed in paragraph [0118].

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nelson et al., 6,974,704, in view of Anderson et al., 6,267,722, and further in view of Friend et al., 6,218,122.

Nelson et al. teach the invention substantially as claimed. Nelson et al. teach the steps of measuring a target antigen and a modified form of the target antigen (see above regarding the discussion of claim 1). Nelson et al. also teach that the analyte concentration can be used to specify the presence or absence of a specific disease or condition (col. 17, lines 51-53). Moreover, Nelson et al. it is apparent that the method can be used for the quantification of more than two analytes for multiple analyte immunoassays (col. 19, lines 38-44). Nelson et al. also teach that the signals from the measurements can be digitized to transfer to a computer (col. 14, lines 33-57, and col. 16, lines 53-56, and col. 18, lines 31-34.)

While Nelson et al. teach the method of measuring the analytes and comparison of the analyte concentration to a concentration that specify the presence or absence of a disease, and that the signals from the measurements can be digitized to transfer to a computer, Nelson et al. do not specifically teach that the computer is used to classify a plurality of different clinical parameters and to generate a classification model classifying a data object to clinical parameter. More specifically, Nelson et al. do not

teach providing a learning set comprising a plurality of data objects representing subjects, wherein the subjects are classified into a plurality of different clinical parameters and wherein each data object comprises data representing specific measurement of a plurality of polypeptides from a subject sample; and training a learning algorithm with the learning set, thereby generating a classification model, wherein the classification model classifies a data object according to clinical parameter.

However, Anderson et al. disclose that signals from a diagnostic test is processed using data processing software employing data reduction and curve fitting algorithms to give either a positive or negative result, or a quantitative determination of the concentration of analyte in the sample, which is correlated with a result indicative of a risk or presence of a disease or disorder and that the entire procedure is automated and/or computer-controlled (col. 3, lines 25-37). While the diagnostic assay of the Nelson et al. invention is different from the Anderson et al., nevertheless, Anderson et al. teach that signals from a diagnostic test can be processed by a software for correlation of the measurement with the presence of a disease or disorder. It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize a computer as taught bay Anderson et al. in the Nelson et al. invention because Anderson et al. teach that the computer is useful in correlate signals from a diagnostic assay, such as the Nelson et al. immunoassay, with the presence of a disease or disorder, as would be desirable for medical purposes. Moreover, one of ordinary skill in the art would have reasonable expectation of success because Nelson et al. teach that the immunoassay results can be digitized to transfer to a computer.

Also, neither Nelson et al. nor Anderson et al. teach using learning sets or algorithms to classify subjects into a *plurality* of different clinical parameters. (Anderson et al. only refers to correlation to a disease or disorder but do not specifically mention that more than one disease or disorder is classified.)

Friend et al. however teach that a computer for determining a level of one or more disease states in a subject comprising a processor and a memory coupled to the processor (col. 32, lines 11-12.) While the diagnostic assay of the Friend et al. invention is different from the assay of the Nelson et al. or Anderson et al. assay, Friend et al. nevertheless teach a computer that determines the level of one or more disease states by determining, for each of the disease states, response profiles and correlating to the levels of each of the disease states (col. 32, lines 11-39). It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Anderson et al., which teaches using a computer to correlate an analyte measurement to a specific disease, such that the computer correlates an analyte measurement to any one of a *plurality* of diseases stored in the computer, as taught by Friend et al. because Friend et al. teach storing information to more than one disease for correlation in an assay. One of ordinary skill in the art would recognize the benefit of convenience in the ability to correlate an analyte measurement (such as the analyte measurement in the Nelson et al. immunoassay) to any one of a variety of diseases.

Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nelson et al., 6,974,704, in view of Lomas et al., 20040029191.

Nelson et al. teach the invention substantially as claimed (see above), except for measurement by SELDI. (Nelson et al. teach that the mass spectrometry is preferably performed with MALDI technique (see col. 12, lines 15-18).

However, Lomas et al. teach that the SELDI technique offers many advantages over other mass spectrometry based assay systems, such as MALDI. Lomas et al. teach for example that the MALDI analysis culminates in a single sample being placed on the probe, whereas in contrast, SELDI analysis culminates in multiple samples being placed on a single probe. Lomas et al. also teach that unlike the probes used in MALDI analysis, the adsorbent chemistries of the SELDI probe retain the molecules of interest, allowing for concentration of the molecule of interest and removal of contaminants that can degrade the spectra. Lomas et al. teach that the ability to retain molecules of interest increases the signal to noise ratio of the analysis (paragraph [0095]). It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the SELDI technique as taught by Lomas et al. in place of the MALDI technique in the Nelson et al. method for mass spectrometry because Lomas et al. teach that the SELDI has advantages over the MALDI such as allowing for multiple samples to be analyzed and reducing the signal to noise ratio, as would be desirable for more accurate results.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ann Y. Lam whose telephone number is 571-272-0822. The examiner can normally be reached on Mon.-Fri. 10-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ann Lam